Prediction of a second local recurrence in surgically treated recurrent brain metastases patients

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Abstract

Background:
Local recurrence is a common occurrence after resection or radiotherapy for brain metastasis (BM). Very little is known about the benefit of (re-)craniotomy in this scenario: does resecting the initial local recurrence (LR1) invariably lead to a second local recurrence (LR2)? This study aimed to analyze the occurrence and predictors of LR2 in BM patients undergoing craniotomy for LR1.

Methods:
Patients were identified from a departmental database at the Brigham and Women's Hospital, Boston, MA. Multivariable logistic regression and Cox regression analysis were performed to identify predictors of the binary occurrence of LR2 (yes/no) and time-to-LR2, respectively. Based on predictors, the subgroup-specific prevalence of LR2 was explored.

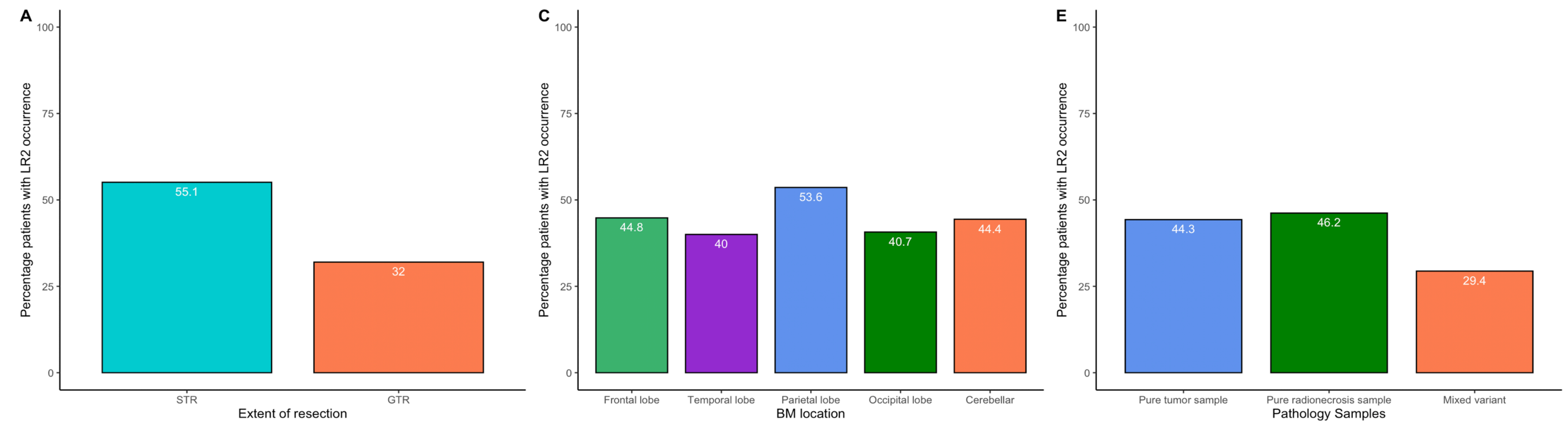
Results:
A total of 188 patients were identified. The median age was 59.5 years and 117 patients (62.2%) were female. Treatment-wise, 76 patients (40.4%) underwent gross total resection (GTR) and 66 (35.1%) received adjuvant radiation. Eighty-one (43.1%) patients experienced LR2 at a median of 7 months after craniotomy. Subtotal resection (STR) (RR = 6.97, p = 0.0008), higher tumor volume (RR = 1.02, p = 0.01), and frontal lobe as location of BMs(RR = 5.13, p = 0.02) were associated with a higher risk of LR2 occurrence. Surgery as treatment for newly diagnosed BM (RR = 0.27, p = 0.04), symptom release (RR = 0.36, p = 0.04), and midline shift (RR = 0.35, p = 0.04) were significantly associated with a lower risk of LR2. Shorter time-to-LR2 was associated with STR (HR = 4.15, p = 0.0003), while mixed variant of radiation necrosis (HR 0.23, p = 0.03), temporal (HR = 0.18, p = 0.006) and parietal (0.13, p = 0.0008) location were associated with longer time-to-LR2. When stratifying by extent of resection, prevalence of LR2 was 32% after GTR and 55.1% after STR.

Conclusion
In this population, LR2 occurred in 43.1% of patients. STR was the most substantial risk factor for LR2, while tumor size, radiation necrosis, location, and surgical treatment of initial BMs may also influence subsequent recurrence.

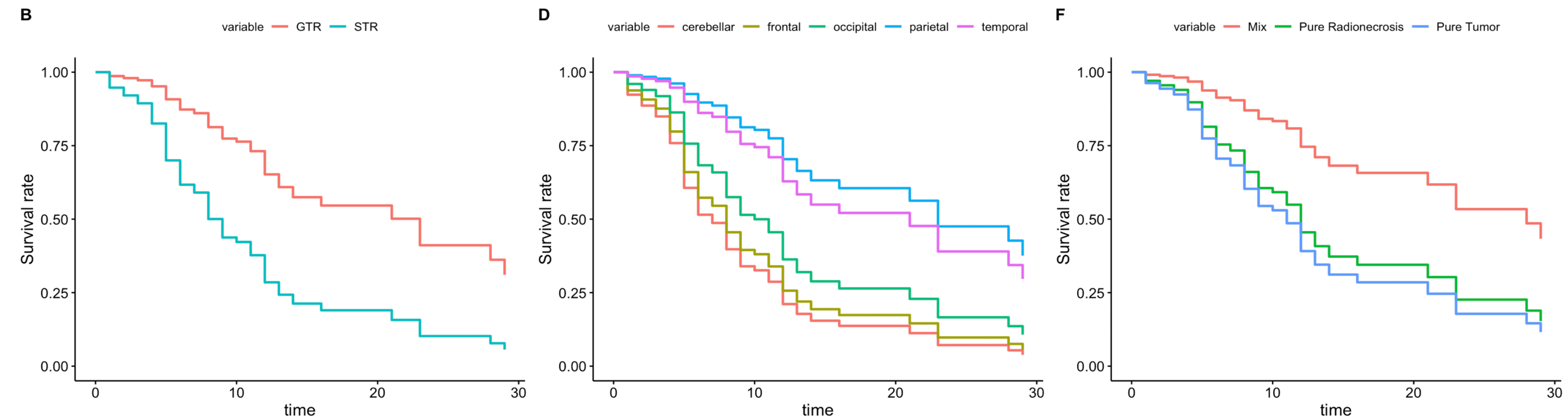
Cox Proportional Hazards Predictors of time to LR2	HR	95% CI	P-value
Age	1.00	[0.98 - 1.03]	0.74
Male Sex	1.43	[0.77 - 2.63]	0.26
Initial treatment of brain metastases (ref: SRS)			
Surgery	0.96	[0.43 - 2.16]	0.92
WBRT	0.35	[0.09 - 1.36]	0.13
Radionecrosis (ref: Pure tumor sample)			
Pure radionecrosis sample (1)	0.78	[0.29 - 2.10]	0.62
Mixed variant (2)	0.23	[0.06 - 0.88]	0.03
Neurological Deficits Symptoms	0.87	[0.39 – 1.93]	0.72
Tumor Volume	1.05	[0.97 - 1.13]	0.24
Midline Shift	0.60	[0.26 - 1.37]	0.22
Dural Adjacency	1.50	[0.79 - 2.86]	0.22
Symptom Release	1.06	[0.54 – 2.10]	0.86
Extent of Resection: STR vs. GTR	4.15	[1.92 - 8.99]	0.0003
Adjuvant for LR1	1.72	[0.89 – 3.34]	0.11
Location of LR (ref: Cerebellum)			
Frontal	0.80	[0.32 – 1.97]	0.63
Occipital	0.50	[0.12 – 2.20]	0.36
Parietal	0.13	[0.04 - 0.43]	0.0008
Temporal	0.18	[0.05 - 0.60]	0.006

Logistic Regression Predictors of LR2	RR	95% CI	P-value
Age	0.99	[0.83 - 0.89]	0.46
Male Sex	0.85	[0.31 - 1.78]	0.71
Initial treatment of BMs (ref: SRS)			
Surgery	0.27	[0.06 - 0.76]	0.04
WBRT	0.32	[0.04 - 2.08]	0.27
Radionecrosis			
Pure radionecrosis sample	0.51	[0.09 - 2.24]	0.40
Mixed variant	0.36	[0.06 - 1.54]	0.22
Neurologic Deficits	2.37	[0.76 - 6.02]	0.10
Tumor Volume	1.02	[0.88 - 0.90]	0.01
Midline Shift	0.35	[0.11 - 0.81]	0.04
Dural Adjacency	1.54	[0.51 - 3.68]	0.39
Symptom Release	0.36	[0.11 - 0.83]	0.04
Extent of Resection: STR vs GTR	6.97	[2.08 - 20.33]	0.0008
Adjuvant for LR1	1.96	[0.76 - 4.52]	0.17
Location of LR1 (ref: Cerebellum)			
Frontal	5.13	[1.17 - 20.17]	0.02
Occipital	0.70	[0.08 - 3.94]	0.72
Parietal	0.38	[0.06 - 1.59]	0.23
Temporal	1.71	[0.32 - 7.18]	0.49

Figures ACE:
Incidence of LR2 stratified by subgroups per significant predictors of time-to-LR2



Figures BDF:
Adjusted covariate survival curves of all significant predictors of time-to-LR2



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Unnecessary diagnostics in neurosurgery: finding the ethical balance

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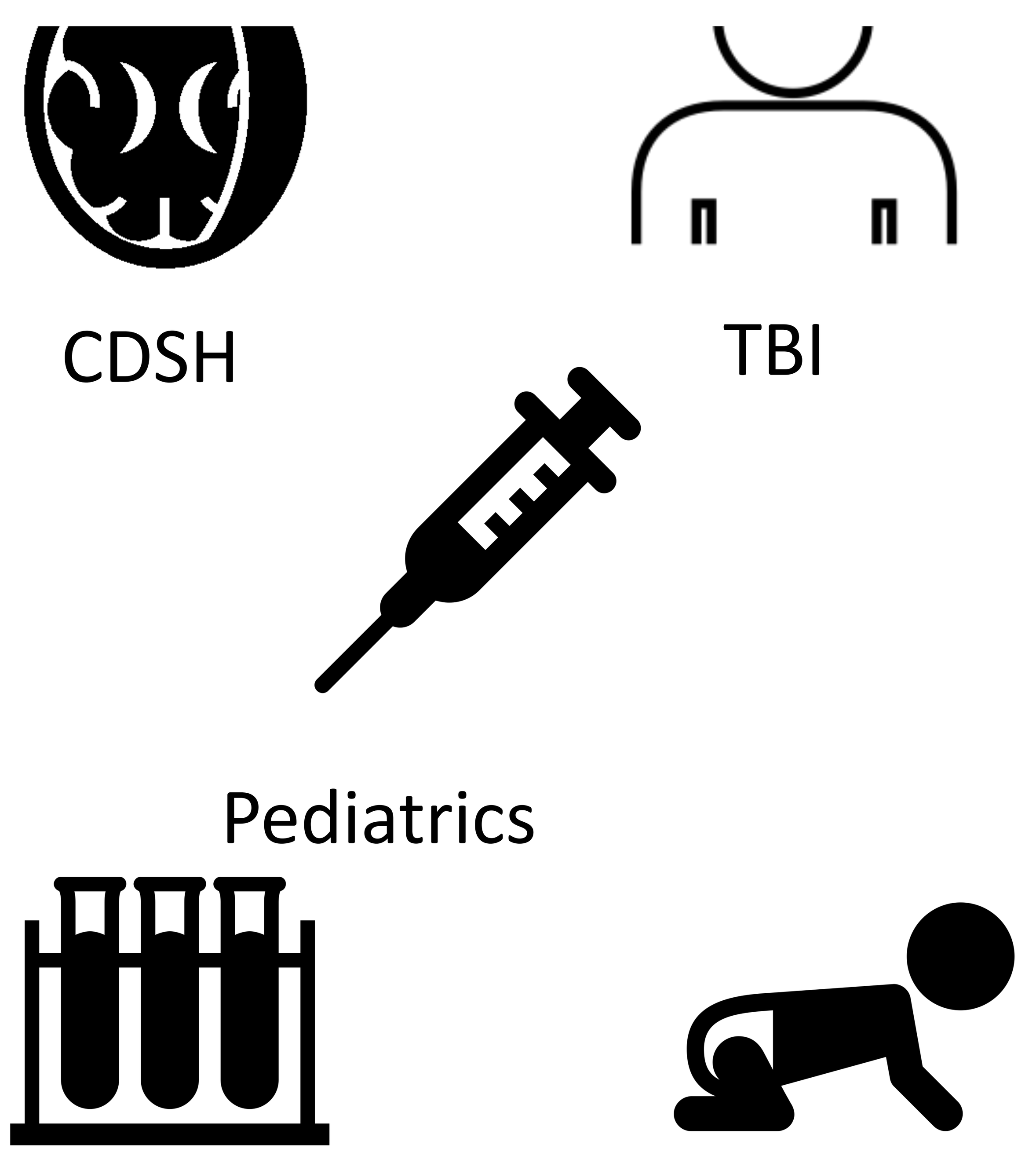
Non-maleficence

- Radiation exposure
- Incidental findings
- Cost/efficiency
- Cultural ingraining



; per 1000 population												
onance imaging	Germany 131	US 118	Japan 112	France 105	Denmark 82	CHE 70	Canada 56	UK 53	NLD 52	Australia 41	Sweden NA	82
mography	US 245	Japan 231	France 197	Denmark 162	Canada 153	Germany 144	Australia 120	CHE 100	NLD 81	UK 79	Sweden NA	151

etween-country variation of imaging use (Papanicolas, JAMA, 2018); partly due utility tests

ing attention towards reducing unnecessary diagnostics, but this has gained traction within neurosurgery

ostic strategy is an ethical balance for the neurosurgeon:

Beneficence

- Diagnostic/prognostic information
- Vulnerable patients → risk-averse strategy
- "Safe > sorry" → defensive practices?

Non-maleficence

- Radiation exposure
- Incidental findings
- Cost/efficiency
- Cultural ingraining

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